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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	Esperester, A. et al.
Serial no.	:	10/262,703
Filed	:	October 2, 2002
Art Unit	:	1617
Examiner	:	Bahar, M.
Attorney Docket No.		1/1109-1-D1

DECLARATION OF UWE GIERLICH, UNDER 37 CFR 1.132

Commissioner of Patents and Trademarks
Washington, DC 20231

Sir:

I, Uwe Gierlich, solemnly state and declare as follows:

1. My technical background is as follows: I am a trained chemist having received a diploma degree in 1988 from the University of Mainz (Germany) and a doctor degree in 1992 from the University of Mainz.

I was employed in the University of Mainz as a scientific assistant until 1995.
From 1987 to 1995 I held positions at the Institute of Inorganic Chemistry and Analytical Chemistry. During these years, I worked in the field of analytical chemistry.

I joined Boehringer Ingelheim in Ingelheim (Germany) in 1995 as a Laboratory Head in the Drug Delivery Department / Development Consumer Health Care.

2. I am familiar with the subject matter of the above-noted patent application.

3. I am familiar with the Office Action dated December 4, 2002 and the prior art cited therein, in particular with Abeles (GB 934,554).

4. In my capacity as laboratory head I supervised the preparation of different extracts of red vine leaves (*vitis vinifera*) and the analysis thereof.

5. In order to demonstrate the difference between the extract according to the present invention and the extract disclosed by the British patent GB 934,554 the following experiments have been carried out:

The red vine leaf extract according to the present invention is prepared by an aqueous extraction at elevated temperature as disclosed in the present application. The process is controlled to gain and maintain a high content of the extract in polyphenols, especially in flavonoids. Flavonoids are considered as a major group of constituents exerting a therapeutic effect in chronic venous insufficiency. The efficacy of said extract has been proven in clinical studies.

The extract described in the British patent is produced by extraction with ethanol, 50 to 80 %, with the addition of inorganic acid. The process is steered to deliver an extract with a high content of anthocyanins, which the patentee of GB 934,554 considered relevant for the effects seen in his pharmacological model.

For a comparison red vine leaves of the same batch were used to produce

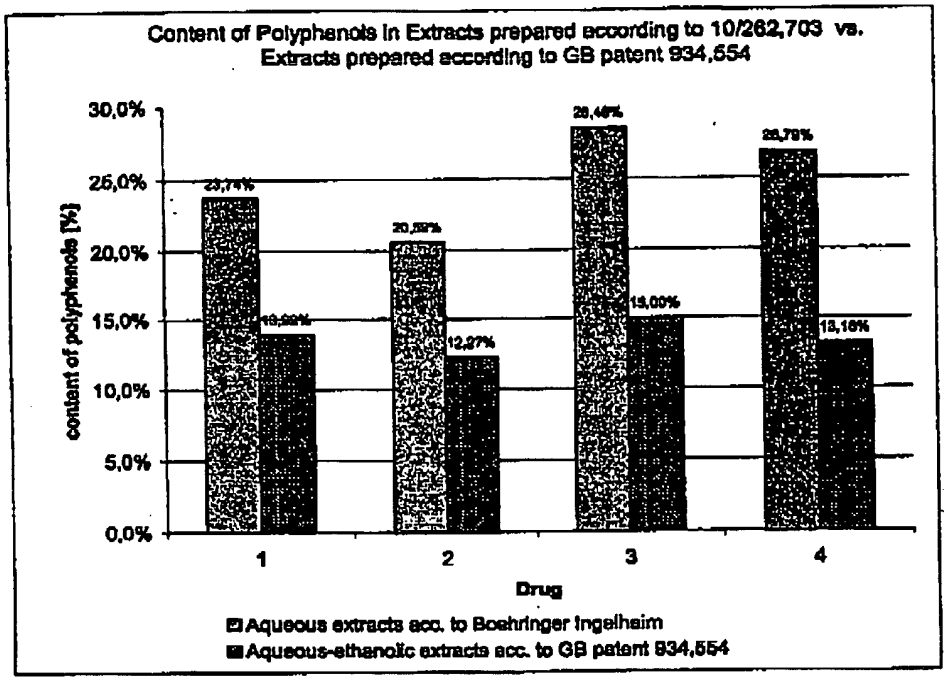
(a) an extract by aqueous extraction, following method disclosed in the present patent application; and

(b) an extract following the instructions laid down in the GB patent 934,554, using average conditions (i.e. extraction with ethanol 65 %, heating at 70-80°C over 45 minutes).

The experiments were repeated four times, using red vine leaves from different grapes and origins.

The resulting extracts were analysed each for their content of anthocyanins, polyphenols and flavonoids. The methods used were validated HPLC-assays for anthocyanins and flavonoids and a pharmacopoeial method for polyphenols. The results are shown in the following tables and diagrams:

Results of the HPLC determination of the polyphenol content:

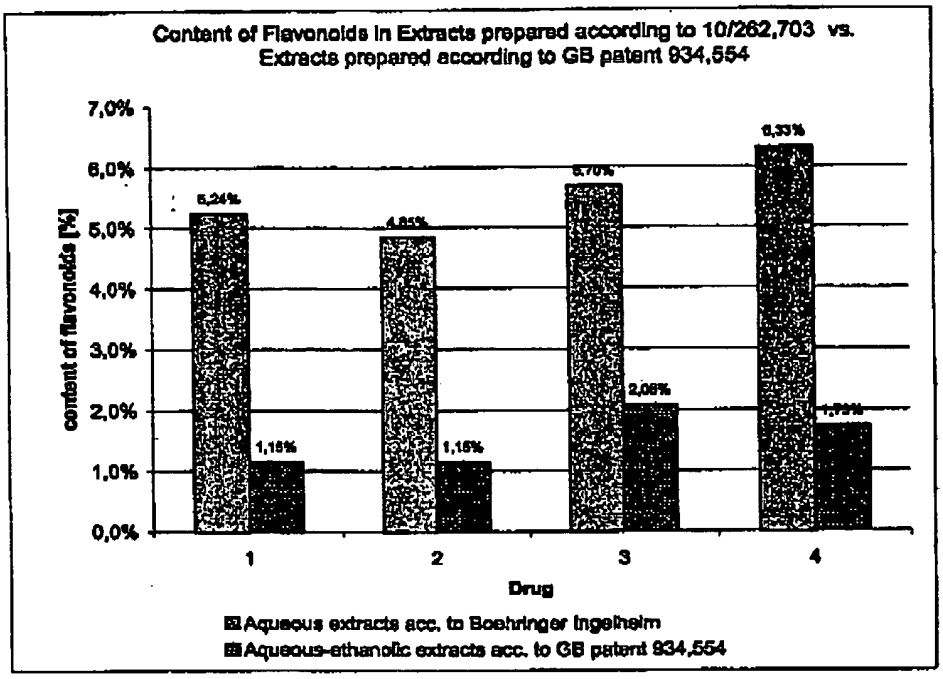


Drug	1		2		3		4	
Extract	BI-1	AB-1	BI-2	AB-2	BI-3	AB-3	BI-4	AB-4
Total polyphenol content	23.7	13.9%	20.6%	12.3%	28.5%	15.0%	26.8%	13.2
Ratio BI / AB	1.7		1.7		1.9		2.0	

BI-1 to BI-4 obtained according to US Ser. No. 10/262,702

AB-1 to AB-4 obtained according to Abeles (GB 934,554)

Results of the HPLC determination of the flavonoid content:

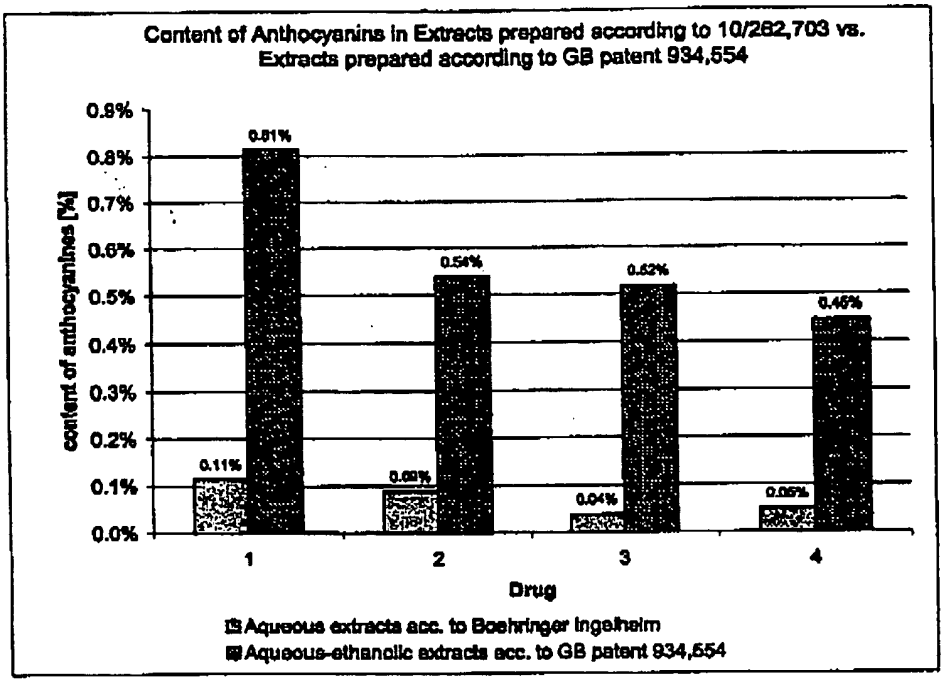


Drug	1		2		3		4	
Extract	BI-1	AB-1	BI-2	AB-2	BI-3	AB-3	BI-4	AB-4
Flavonoid content	5.24%	1.15%	4.85%	1.15%	5.70%	2.08%	6.33%	1.73%
Ratio BI / AB	4.6		4.2		2.7		3.7	

BI-1 to BI-4 obtained according to US Ser. No. 10/262,702

AB-1 to AB-4 obtained according to Abeles (GB 934,554)

Results of the HPLC determination of the anthocyanins contents:



Drug	1		2		3		4	
Extract	BI-1	AB-1	BI-2	AB-2	BI-3	AB-3	BI-4	AB-4
Anthocyanins content	0.11%	0.81%	0.09%	0.54%	0.04%	0.52%	0.05%	0.45%
Ratio BI / AB	0.14		0.16		0.07		0.11	

BI-1 to BI-4 obtained according to US Ser. No. 10/262,702

AB-1 to AB-4 obtained according to Abeles (GB 934,554)

The aqueous extraction yields products with a high content of polyphenols and especially of flavonoids, 3 to 5 fold as much as in an extract prepared according to the method described in the British patent.

The extract according to GB patent 934,554, on the other hand, is rich in anthocyanins. The amount is about 6 to 10 fold higher than that of the inventive extract.

The comparison shows that both the extraction methods lead to extracts with totally different compositions.

The undersigned petitioner declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: 24.02.2003 Signature: _____
Name